(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
24 February 2005 (24.02.2005)

PCT

(10) International Publication Number
WO 2005/016868 A3

(51) International Patent Classification[7]: C07C 235/00, 255/00

(21) International Application Number: PCT/EP2004/009087

(22) International Filing Date: 12 August 2004 (12.08.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0319069.1 14 August 2003 (14.08.2003) GB

(71) Applicant *(for all designated States except US)*: **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford Middlesex UB6 0NN (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **HOLMES, Ian** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). **WATSON, Stephen, Paul** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB).

(74) Agent: **QUILLIN, Helen**; GlaxoSmithKline, Corporate Intellectual Property, 980 Great West Road, Brentford Middlesex TW8 9GS (GB).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

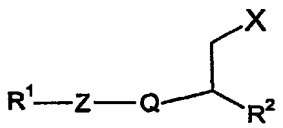
(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report: 19 May 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MATRIX METALLOPROTEINASE INHIBITORS



(I)

(57) Abstract: Compounds of Formula (I), wherein R^1 represents optionally substituted -C_{4-12} alkyl, -C_{2-10}alkylcycloalkyl, -C_{2-6} alkyl heterocycloalkyl, -C_{2-6}alkylaryl, optionally substituted 5- or 6- membered aryl or heteroaryl, except pyridinyl. Z represents a bond, CH_2, O, S, SO, SO_2, NR^4, OCR^4R^5, CR^4R^5O, or Z, R^1 and Q together form an optionally substituted fused tricyclic group; Q represents an optionally substituted 5- or 6- membered aryl or heteroaryl ring; X represents COR^3; R^2 represents $CONH_2$, CO_2H, CO_2R^7, SO_2R^7 or $SO_2NR^8R^9$, except that R^2; may not represent CO_2R^7 when X is $CONH_2$; R^3 represents OR^6, or NR^8R^9; R^4 and R^5 each independently represents H, C_{1-6} alkyl or C_{1-4} alkylaryl; R^6 represents H or C_{1-6} alkyl; R^7 represents C_{1-6} alkyl; R^8 and R^9 each independently represents H or C_{1-6} alkyl or R^8 and R^9 together with the nitrogen atom to which they are attached form a 5- or 6- membered ring which may optionally include 1 or more further heteroatoms selected from O, S and N; and physiologically functional derivatives thereof with the exception of [3-(acetylamino)-4-cyclohexylphenyl]-butanedioic acid and 3-(acetylamino)-4-cyclohexylphenyl]-butanedioic acid diethyl ether; butanedioic acid [3-methoxy-4-(phenylmethoxy)phenyl]; butanedioic acid [4-(phenylmethoxy)phenyl]; with the proviso that when R^1 represents C_{4-12} alkyl, Z is other than a bond, O or CH_2; and physiologically functional derivatives thereof , processes for their preparation, pharmaceutical formulations containing them and their use as inhibitors of matrix metallproteinase enzymes (MMPs) are described.

WO 2005/016868 A3